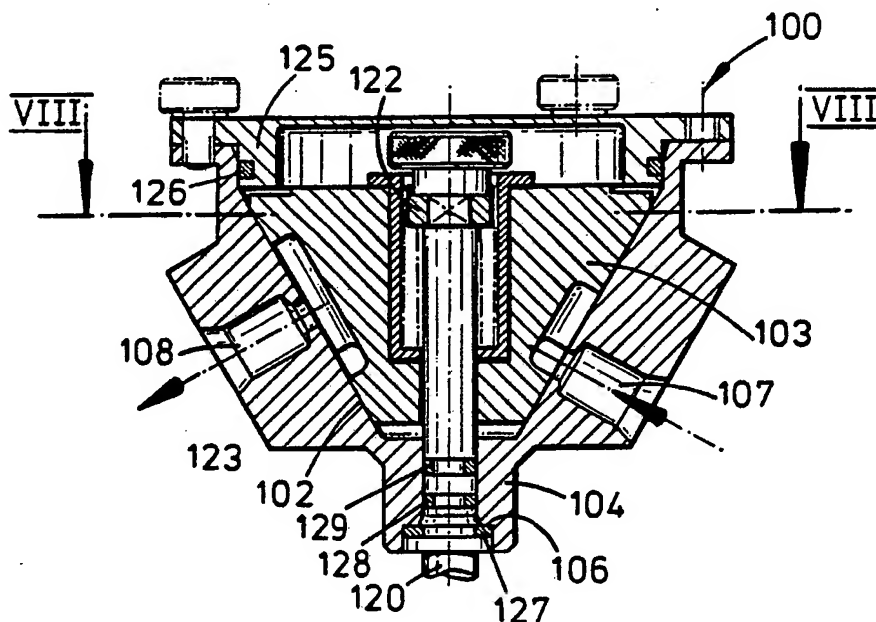




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: PCT/GB89/00857</p> <p>(22) International Filing Date: 7 July 1989 (07.07.89)</p> <p>(71) Applicants (for all designated States except US): THE UNIVERSITY OF MANCHESTER INSTITUTE OF SCIENCE & TECHNOLOGY [GB/GB]; P.O. Box 88, Sackville Street, Manchester M60 1QD (GB). APRIL COMPUTING EXECUTIVE LIMITED [GB/GB]; Chestnut Farm, Tarvin Road, Frodsham, Cheshire WA6 6XN (GB). NORMEC (MANCHESTER) LIMITED [GB/GB]; Alpha Works, Smalley Street, Rochdale OL11 3EB (GB).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): FARIA, Julio, F. [CA/GB]; Eversley End, Hazelhurst Road, Frodsham, Cheshire WA6 6EX (GB). MARSHALL, Robert, D. [GB/GB]; Cae Rhenallt Farm, Ffrith, Wrexham, Clwyd (GB). PEARSON, Robert, C. [GB/GB]; PEARSON, Stephen, C. [GB/GB]; Normec (Manchester) Limited, Smalley Street, Castleton, Rochdale OL11 3EB (GB). PEPPER-CORN, Duncan [GB/GB]; Ivy House, Smith's Lane, Weaverham, Cheshire CW8 3HF (GB). WEBB, Colin [GB/GB]; "Ingleside", Park Road, Hadfield, Hyde, Cheshire SK14 8AH (GB). DEAN, Jonathan, Fraser [GB/GB];</p>	<p>12 Booth Court, Ellison Street, Glossop, Derbyshire SK13 8BU (GB).</p> <p>(74) Agent: ATKINSON, Peter, Birch; Marks & Clerk, Suite 301, Sunlight House, Quay Street, Manchester M3 3JY (GB).</p> <p>(81) Designated States: AT, AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CM (OAPI patent), DE, DE (European patent), DK, FI, FR (European patent), GA (OAPI patent), GB, GB (European patent), HU, IT (European patent), JP, KP, KR, LK, LU, LU (European patent), MC, MG, ML (OAPI patent), MR (OAPI patent), MW, NL, NL (European patent), NO, RO, SD, SE, SE (European patent), SN (OAPI patent), SU, TD (OAPI patent), TG (OAPI patent), US.</p> <p>Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments. Before the expiration of the time limit referred to in Article 21(2)(a) on the request of the applicant. With a request for rectification under Rule 91.1(f).</p>	

(54) Title: METHOD AND APPARATUS FOR SAMPLING



(57) Abstract

Sampling apparatus (100) comprises a housing (101) having a plurality of circumferentially spaced sample ports (109) extending through a wall of the housing. A distributor member (103) is rotatably mounted in a sealed bore (102) of the apparatus. The apparatus has a fluid inlet (107) through which fluid from a reaction vessel may enter the apparatus and a fluid outlet (108) through which fluid may be recirculated back to the vessel. The distributor member (103) has conduit (110, 111) adapted to provide selective communication between the fluid inlet (107) and any one of the sampling ports (109).

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METHOD AND APPARATUS FOR SAMPLING

The present invention relates to a method and apparatus for sampling, particularly but not exclusively for obtaining samples from a biological or bio-technological reaction process, e.g. fermentation.

Various apparatus are already known for taking samples at predetermined intervals of the time from a biological or bio-technological reaction process for subsequent analysis so that the progress or course of the reaction may be followed. One such apparatus comprises a tube providing a loop through which reaction media may pass from and back to the reaction vessel. A sampling arrangement is provided in the loop and comprises a number of sampling outlets each with a sampling valve which is opened at the appropriate time to discharge material into a sample tube. Such apparatus is however difficult to maintain sterile, particularly because of the large number of valves. Sampling apparatus is also known which includes a carrousel or other support for holding sampling tubes (or the like) which are indexed past a sampling outlet of the apparatus and which collect samples at desired intervals. Generally an ultra-filtration membrane is incorporated in the apparatus through which the sample must pass. This membrane is intended to maintain sterile conditions in the apparatus. However a disadvantage of such apparatus is that it is difficult to sterilise and furthermore may only be used for obtaining samples of the liquid in the reaction medium since the ultra-filtration medium prevents passage of the cells into the sampling tube. In many instances, particularly in research work, it may be desired to obtain samples containing cells and

this is not possible with the conventional apparatus.

According to a first aspect of the invention there is provided sampling apparatus comprising a housing having a plurality of circumferentially spaced sample ports extending through the wall thereof, a distributor member rotatably mounted in a sealed bore of the apparatus, a fluid inlet through which fluid from a vessel may enter the apparatus a fluid outlet which may communicate with the inlet so that fluid may be returned to the vessel said distributor member having conduit to provide selective communication between the fluid inlet and any one of the sampling ports, and means for effecting rotation of the distributor member.

The sealing registration of the aperture in the wall of the distributor member with the sample outlet apertures may be ensured by having the distributor member and the wall of the bore of material which facilitates this sealing. For example the distributor member may be of PTFE whereas the housing may be of stainless steel.

The outer surface of the distributor member and the wall of the bore may be of complementary frustoconical configuration.

Preferably the outer face of the distributor member has a channel arrangement which is capable of selectively providing communication between the fluid inlet and a sampling port with simultaneous closure of the outlet port by a face of the distributor and is further capable of (upon rotation of the distributor member) of selectively providing communication between the fluid inlet and the fluid outlet with simultaneous closure of the sampling ports by the faces of the distributor.

In an alternative arrangement, the distributor member has a sample holding chamber which communicates

with said fluid inlets and outlets and which further has an aperture in a wall thereof. This aperture may be selectively brought in to sealing registration with any one of the sample outlet apertures by rotation of the distributor member so that fluid in the sample holding chamber may pass through a sampling port.

A peristaltic pump may be used to circulate fluid from the reaction medium through the chamber.

Preferably the means for effecting rotation of the distributor member is a drive shaft or the like which is axially non-moveable since such axial movement provides the possibility of contaminant material (eg. air-borne bacterial entering the apparatus).

Preferably also the distributor member is spring biased into the housing.

According to a second aspect of the invention there is provided a method of obtaining a sample from a reaction medium, for example a biological or biotechnological reaction medium, comprising passing fluid from the reaction medium to the inlet of a sampling apparatus having a rotatable distributor member capable of selectively providing communication between the inlet and any one of a plurality of spaced sample outlet apertures in a housing in which the distributor member is rotatably mounted, and rotating said distributor member so that it provides said communication between the inlet and a sample outlet when it is desired to take a sample of the reaction medium.

Preferably the fluid from the reaction medium is passed through the sampling apparatus and recirculated back to the reaction medium at least during the time when a sample is not being taken.

Preferably the reaction medium comprises bacteria or other cells which are collected in the

sample.

The invention will be further described by way of example only with reference to the accompanying drawings, in which:

Fig. 1 is a sectional view of one embodiment of sampling apparatus in accordance with the invention;

Fig. 2 is a detail of Fig. 1 showing the apparatus in a condition for taking a sample; and

Fig. 3 illustrates an arrangement of sampling tubes around the apparatus.

Fig. 4 is a side view of a further embodiment of sampling apparatus in accordance with the invention, but omitting details of the inlet port, the outlet port, and the sampling ports for the purpose of clarity;

Fig. 5 is an underside view of the apparatus shown in Fig. 4;

Fig. 6 is a section on the line VI-VI of Fig. 5;

Fig. 7 is a section on the line VII-VII of Fig. 5;

Fig. 8 is a section on the line VIII-VIII of Fig. 7;

Fig. 9 illustrates the plug used in the apparatus of Fig. 4; and

Fig. 10 illustrates a cup as used in the apparatus of Fig. 4.

Referring to Fig. 1, the illustrated sampling apparatus 1 comprises a generally cylindrical body 2 formed with a central bore 3 closed by upper and lower end cap assemblies 4 and 5 respectively. Intermediate its upper and lower sections 3a and 3c respectively, the bore is of upwardly tapering frustoconical configuration, as referenced by 3b.

Provided within bore 3 is a rotatable distributor member 6 of PTFE. This member has an outer frustoconical face 6a which is a close sealing fit within the section 3b of bore of body 2 such that

there will be no ingress of sampled material between these two sections. A well 7 is formed in the upper part of distributor member 3 which further has a single bore 8 (Fig 2) at a level above the floor of the well. This bore 8 is intended to be selectively registrable (as described more fully below) with any one of a twelve equiangularly spaced bores 9 provided in the body 2 (see also Fig. 3).

Extending through the lower end-cap assembly 5 is a drive shaft 10 terminated within the body 2 by a cruciform end section 11 which locates in a complimentary cruciform recess (not shown) provided in the floor of a circular recess 6b in the base of the distributor member 6. Shaft 10 is associated with a drive mechanism (not shown) capable of rotary indexing distributor member 6 for the purpose to be described. The inter-engaging cruciform configurations ensure that axial forces exerted by the drive mechanism are not transmitted to the distributor member.

Three equiangularly spaced plungers 12 are slidable in respective apertures provided in the end cap assembly 5 and are biased inwardly of the body 2 by coil springs 13 located in ports 14 affixed to the outer surface of the cap-assembly 5. These plungers 12 serve to urge an annular plate 15 against the undersurface of the cruciform end section 11 of the drive shaft and the undersurface of the body 2 so as to retain the former in position and also to urge the distributor member 6 into the bore 3. Additionally three equiangularly spaced pins 16 are fixed on plate 15 and extend with slight clearance through apertures 17 in the end-cap 5. Circlips 18 or the like on the ends of pins 16 prevent the latter from being fully withdrawn from the end-cap. Thus the end-cap assembly may be removed from the apparatus as one unit with the plate 15.

The upper end cap assembly 4 has a central spigot 4a which extends part way into well 7. An O-ring 19 provides a seal between the spigot 4a and the inner wall of the well.

Extending through the end cap assembly 4 into well 7 are two tubes 20 and 21 both of which communicate with a fermentation vessel (not shown) for which a sample is to be taken.

A peristaltic pump (not shown) serves to pass 'broth' from the fermentation vessel continuously along tube 20 into well 7 and then back along tube 21.

Located in each bore 9 is a right-angled outlet tube 22 on which a sample tube (not shown) may be mounted. Twelve such outlet tubes 22 are provided (see Fig. 3) one for each aperture 9. Flats 23 on the outlet tube 22 prevent unwanted rotation thereof relative to the body 2 such as might otherwise occur due to the indexing of the distributor member 6.

In use of the apparatus, broth from the fermentation vessel is continuously circulated through the well 7. During the period of time when sampling is not required, the distributor member 6 is at a position in which its bore 8 is between two of the apertures 9 in the body 2. Leakage of broth between the distributor 6 and the body 2 is prevented as a result of the close fit between these two components. When a sample is to be taken, distributor member is indexed around so that its bore 8 registers with a bore 9. Thus 'broth' passes into the associated sample tube. After a predetermined length of time (governed by the time taken to collect a sample of the required volume) the distributor member 6 is indexed further round so that its bore 8 is again out of register with a bore 9. Obviously when a further sample is required, the distributor member 6 is again indexed so that its bore 8 registers with the next

bore 9 in sequence. With the illustrated apparatus, the sampling procedure may be carried out a total of twelve times.

The apparatus may of course be under computer control to effect sampling over a prolonged time period. Each sample tube may incorporate any suitable chemical to arrest the fermentation reaction at the point when that sample was taken. Thus the sample is 'frozen' for subsequent analysis. The illustrated apparatus has a number of advantages, namely:

1. Aseptic conditions are readily maintained.
2. There will be no stagnation in the bore 8 and/or 9.
3. Sampling of whole 'broth' (i.e. including cells) is possible whilst maintaining aseptic conditions. (This is not possible in prior art sampling arrangements where ultra-filtration membranes required to maintain aseptic conditions prevent whole cell sampling).
4. The apparatus may be easily sterilised either in an autoclave or by steam sterilisation (i.e. passing steam through tubes 20 and 21)
5. The apparatus is easy to assemble and dismantle and therefore easy to clean.

Although the apparatus has been described with specific reference to collection of samples in sample tubes, it should be appreciated that one or more further units 1 may be provided as 'satellites' to the illustrated unit. Each such further unit will be in communication with a respective bore 9 of the 'base'

unit. A sample at time T_1 may be passed to satellite unit S, in which the sample is allowed to continue fermentation. Sample may then be taken from S, at time intervals T_{2-13} (assuming twelve bores 9 on S1). Similarly a sample may be taken from the base unit at time T_{14} and passed to satellite S2 for further sampling at times of T_{15-26} . Similarly for other satellite units. Thus with a total of twelve satellite units, it is possible to take 144 samples at different time intervals.

The sampling apparatus 100 illustrated in Figs. 4 to 8 comprises a stainless steel body 101 with a downwardly tapering bore 102 in which a complementary frustoconical distributor plug 103 is rotatably mounted. The body 101 itself has one open end (ie. that end adjacent the wider end of bore 102) and at the other end is extended by a nose 104. Within this nose 104 is a bore 105 which is coaxial with bore 103 and which (in going from the free end of the nose towards bore 102) is narrowed by a step 106.

Provided within the walls of the body 101 surrounding the bore 102 are a plurality of downwardly and outwardly inclined ports as follows:

- a) an inlet port 107 towards the lower end of bore 102;
- b) an outlet port 108 higher up the bore 102 than the inlet port 107 and spaced around the body by 180° therefrom; and
- c) twelve equiangularly spaced sampling ports 109 which are above the level of the outlet port 108 (see Fig. 3).

The sampling ports 109 are thus spaced by 30°

from each other (see Fig. 5) around the body 101. Additionally, the inlet and outlet ports 107 and 108 (which are spaced by 180° from each other) are each spaced by 15° from the adjacent sampling ports.

The distributor plug 103 is of PTFE which ensures that its outer frustoconical surface is a sealing fit within the bore 102. The general configuration of the plug 103 is shown in Fig. 9 and will be seen to include a lower annular channel 110 which, when the plug is in the bore 102, is at the level of the inlet port 107 (see Fig. 7). Communicating with channel 109 is a finger like sub-channel 111 which extends along the frustoconical face from the channel 110 towards the upper end of the plug 103. The length of sub-channel 111 is such that with the plug 103 seated in bore 102, the upper end of the sub-channel 111 is capable of registering with a sampling port 109. Additionally, a further eleven finger sub-channel 112 are provided in plug 103 each communicating at their lower ends with annular channel 110. These sub-channels 112 are generally similar to the sub-channel 111 but are of a length such that they extend only to the level of the outlet port 108, the height of which has been indicated in chain-dot-line in Fig. 6.

There are a total of twelve of the finger-like sub-channels (eleven sub-channels 112 and one sub-channel 111) equiangularly disposed around plug 103.

The function of the channel 110 and the sub-channels 111, 112 will be described in more detail below.

Extending centrally within plug 103 is a bore which, in going from lower to the upper (as viewed in Fig. 7) of the plug is formed in two successively widening sections 113 and 114. At its upper end, bore 114 opens into a rectangular slot 115 (see also Fig.

8). Seated in bore section 114 is a cylindrical cup

116, of which a more detailed view is shown in Fig. 10. It will be seen that this cup has, towards its upper end, two diametrically opposed cut-outs 117 which are of a depth such that, with the cup 116 seated in the bore 116, they extend over the height of the slot 115. Cup 116 also has an upper annular flange 118 as shown and an aperture 119 in its base.

The rotatable mounting of the plug 103 is by means a vertically fixed drive shaft 120. This shaft extends upwardly through the nose 104 of body 101 and centrally through the plug 103 and cup 116.

At its upper end, the shaft is screw-threaded (not shown) and just below these screw threads it has a square section 121 (see also Fig. 8). A rectangular key 122 is mounted on the square section 121 and is located in slot 115 with which it makes line contact. The height of key 122 is less than the depth of slot 151 for reasons which will be described below.

Key 122 is retained in position on shaft 120 by a spindle nut 123 provided on the screw threaded end of the shaft. This nut 123 prevents vertical movement of key 122 in a direction parallel to the axis of shaft 120.

It will be appreciated that rotation of shaft 120 drives the plug 103 via key 122. Nevertheless, the fact that key 122 makes line contact in slot 115, it is possible for the plug 103 to move vertically relative to the bore 102. A coil spring 124 is provided in the cup 116 and serves normally to urge the plug 103 downwardly into the bore 102.

An end plate 125 is fixed on the open end of body 101 and incorporates a seal 126. Further seals 127 to 129 are provided as shown for sealing the shaft 120 within the nose 104.

In use of the apparatus, sample tubes (not shown) are mounted in each of the sampling ports 109 by means

of adapters 130 (see the insert to Fig. 4) which are associated with seals 131. Additionally, the inlet and outlet ports 107 and 108 are connected to a fermenter, and a peristaltic or other constant volume pump (not shown) is provided for supplying the medium from the fermenter to the sampling apparatus. Seals (not shown) will also be provided at the inlet and outlet ports. These seals, together with the seals 127-129 and 131, prevent contamination of the interior of the sampling apparatus by the surrounding air.

Assume now that medium from the fermenter is being passed to the sampling apparatus and that it is desired merely to re-circulate the medium back to the fermenter without taking a sample. In this case, the plug may be positioned so that any one of the sub-channels 112 is in register with the outlet port 108. Medium entering the inlet port 107 will enter the annular channel 110 (which is at the level of the port) and will pass along this channel and then exit through the outlet port 108 via the sub-channel 112 registering therewith. It will be appreciated that the sub-channel 111 is located between two of the sampling ports 109 which are therefore closed by those faces of the plug 103 between the sub-channels (see the left hand insert to Fig. 4.) Thus, none of the medium passes to a sample port 109.

Consider now that it is desired to take a sample. The shaft 120 (driven by a motor - not shown) is indexed round by 15°. This brings sub-channel 111 into register with one of the sampling ports 109 (see the right hand insert on Fig. 4). Additionally the outlet port 108 is now closed off by the face of the frustoconical plug so that medium cannot pass therethrough. The plug is maintained in this position for sufficient time to collect the required sample.

The plug is now indexed round by a further 15° so

as to bring a further sub-channel 112 into register with the outlet, and to close off the sampling ports 109. Samples may be collected through all twelve sampling ports 109 by indexing the plug around in 15° increments in accordance with the above described procedure. It will be appreciated that at some stage during this procedure, the sub-channel 111 comes into register with the outlet port 109. This is the condition illustrated at the left hand side of Fig. 7.

In this case, the medium is able to pass through outlet port 108 via the sub-channel 112.

The sampling apparatus illustrated in Figs. 4 to 8 has the following advantages.

(i) the angular contact between the plug 103 and the bore 102 (of the body 101) gives a low coefficient of the friction;

(ii) since the fluid entering at the inlet 107 flows through the apparatus, either to outlet port 108 or a sampling port 109, there is no stagnation of fluid within the apparatus;

(iii) the apparatus is of compact construction, and can therefore be readily autoclaved.

(iv) during autoclaving, the plug is able to move up against spring 124 so as to cater for the differential expansion between the stainless steel body 101 and the PTFE plug 103;

(v) since the liquid flow around the distributor member generates an upward force only over a comparatively small area, it is possible for the medium being supplied to the apparatus to be at comparatively high pressure whilst there is only a generated on the distributor member. It is thus possible to use low torque drive of means small size with the result that the apparatus is of compact construction; and

(vi) since the outlet is closed whilst liquid is

being passed through a sample port, all of the pressure of supply of the liquid to the apparatus is used in causing the liquid to flow out through the sampling port (if the apparatus of Figs. 1 to 3 in which liquid continues to recirculate through the apparatus during sampling)

CLAIMS

1. Sampling apparatus comprising a housing having a plurality of circumferentially spaced sample ports extending through the wall thereof, a distributor rotatably mounted in a sealed bore of the apparatus, a fluid inlet through which fluid from a vessel may enter the apparatus, a fluid outlet which may communicate with the fluid so that fluid may be returned to the vessel said distributor member having conduit adapted to provide selective communication between the fluid inlet and any one of the sampling ports, and means for effecting rotation of the distributor member.

2. Apparatus as claimed in Claim 1 wherein the inlet and outlet ports are provided in the housing.

3. Apparatus as claimed in Claim 2 wherein the outer face of the distributor member has a channel arrangement capable of selectively providing communications between the inlet and a sampling port with simultaneous closure of the outlet port by a face of the distributor and is further capable of selectively providing communication between the inlet and the outlet with simultaneous closure of the sampling ports by the faces of the distributor.

4. Apparatus as claimed in Claim 4 wherein the outlet port is at a level intermediate that of the inlet port and the sampling ports, and the distributor member has a circumferentially extending main channel at the level of the inlet and a plurality of first sub-channel, and a second sub-channel each communicating with main channel and extending transversely thereto along the face of the distributor member, said first sub-channel extending to the level of the outlet and said second sub-channel extending to the level of the sampling ports, the angular

disposition of the sub-channel around the distributor being such that communication between the inlet and outlet is interrupted when the second sub-channel is in register with a sampling port and that there is no communication between the inlet and a sampling port when the outlet is in register with a first or the second sub-channel.

5. Sampling apparatus as claimed in Claim 1 wherein said distributor member has a sample holding chamber which communicates with said inlet and outlet and further has an aperture in its wall which aperture may be selectively brought into sealing registration with any one of the sample outlet apertures by rotation of the distributor member.

6. Apparatus as claimed in any one of Claims 1 to 5 wherein the distributor member and the bore are frustoconical.

7. Apparatus as claimed in Claim 6 wherein the distributor member is axially movable within the bore and is spring biased to its sealed position.

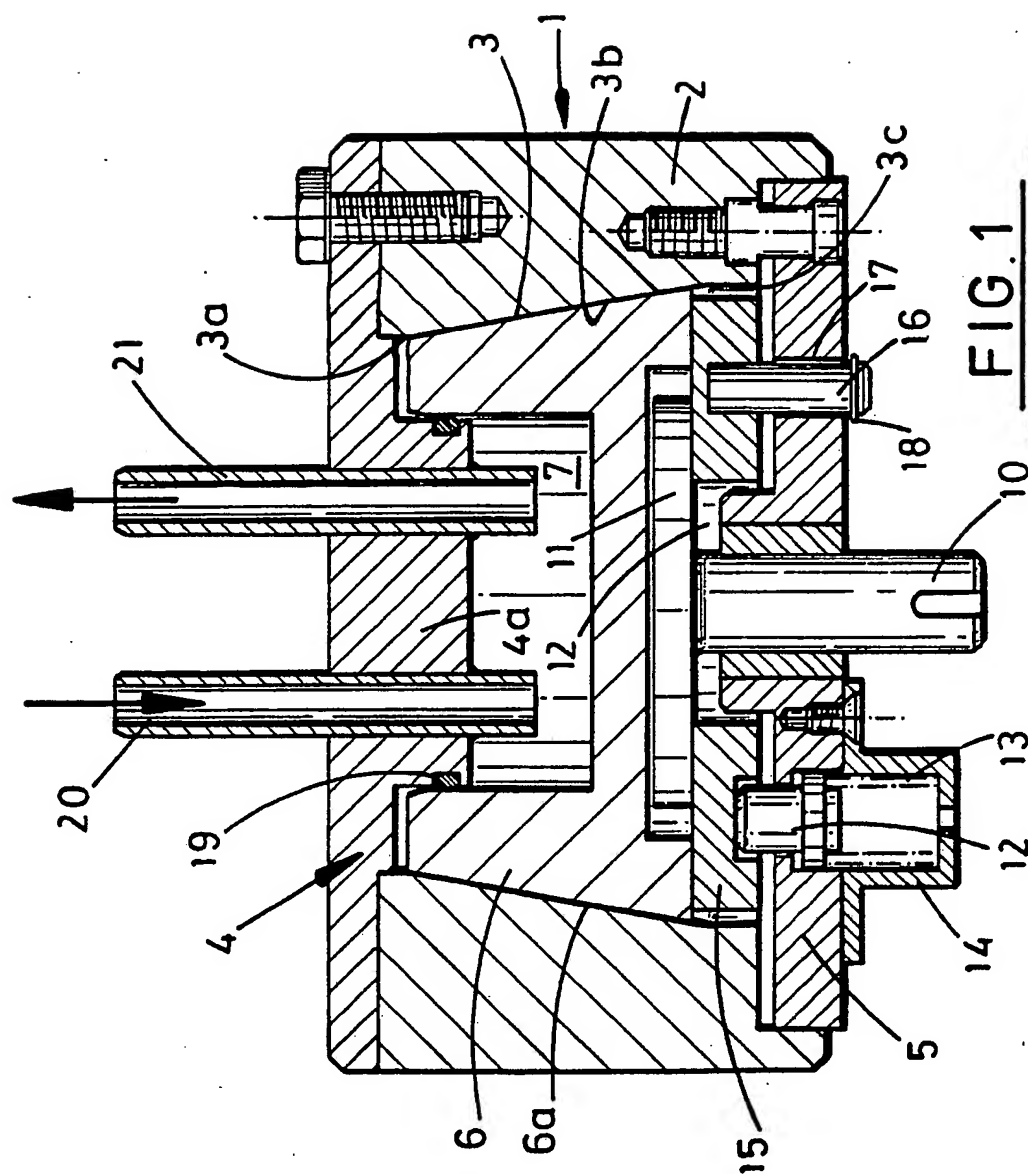
8. Apparatus as claimed in any one of Claims 1 to 7 wherein the housing is of metal and the distributor member is of PTFE.

9. A method of obtaining a sample from a reaction medium, for example a biological or biotechnological reaction medium, comprising passing fluid from the reaction medium to the inlet of a sampling apparatus having a rotatable distributor member capable of selectively providing communication between the inlet and any one of a plurality of spaced sample outlet apertures in a housing in which the distributor member is rotatably mounted, and rotating said distributor member so that it provides said communication between the inlet and a sample outlet when it is designed to take a sample of the reaction

medium.

10. A method as claimed in Claim 9 wherein the fluid from the reaction medium is passed through the sampling apparatus and recirculated back to the reaction medium at least during the time when a sample is not being taken.

11. A method according to Claim 9 or 10 wherein the reaction medium comprises cells or bacteria which are collected in the sample.



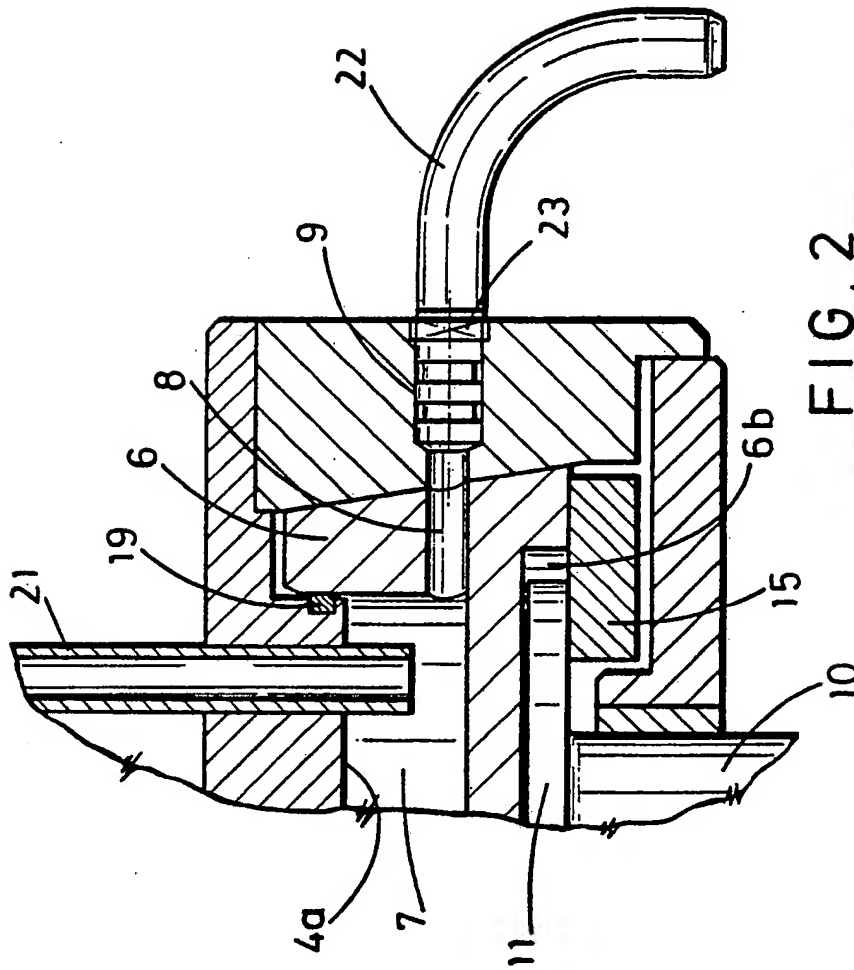


FIG. 2

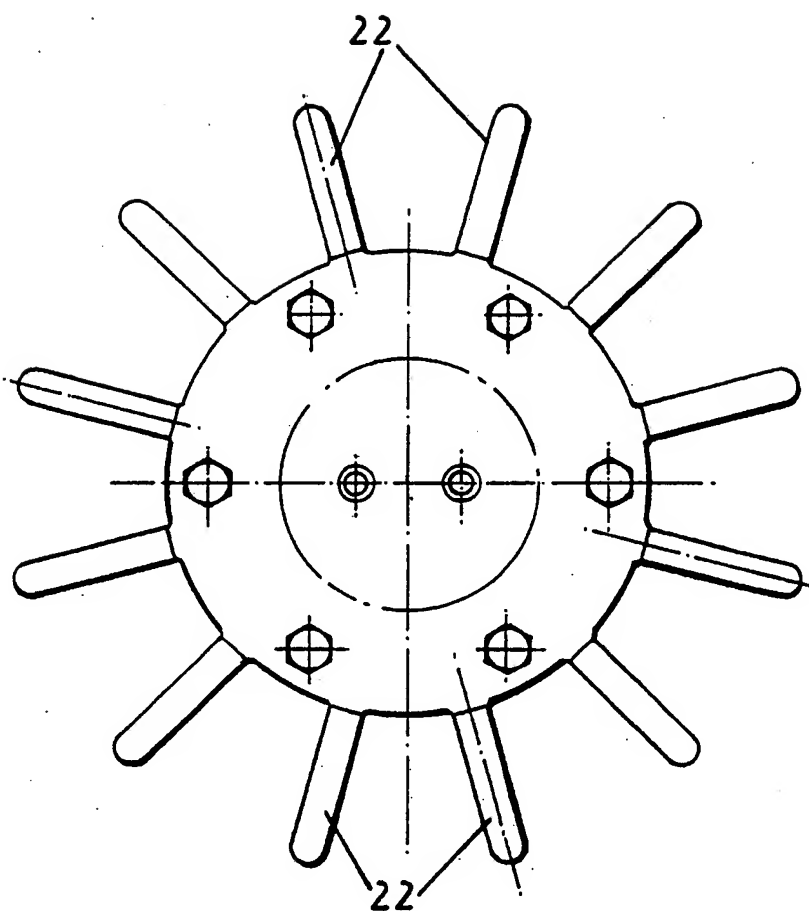
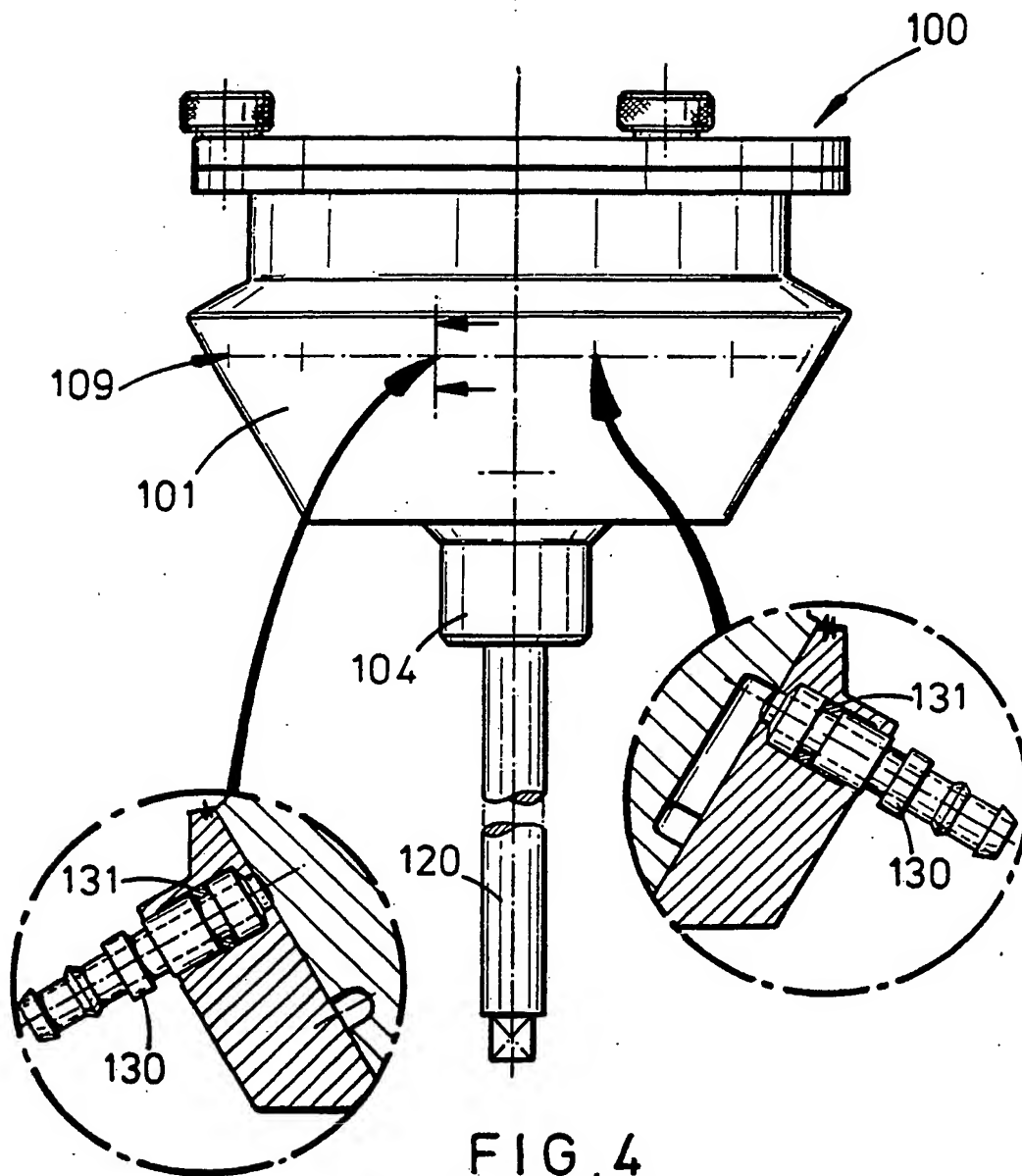


FIG. 3

FIG. 4

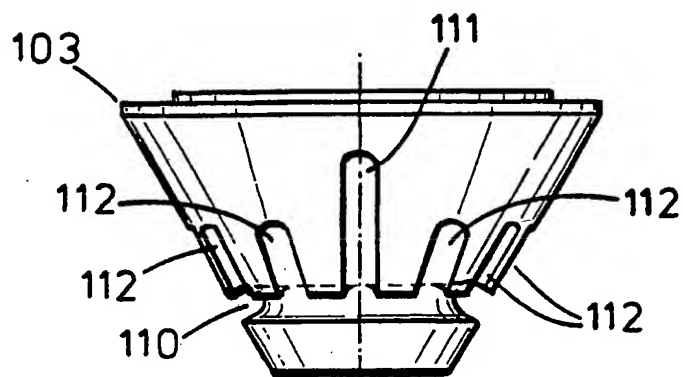


FIG. 9

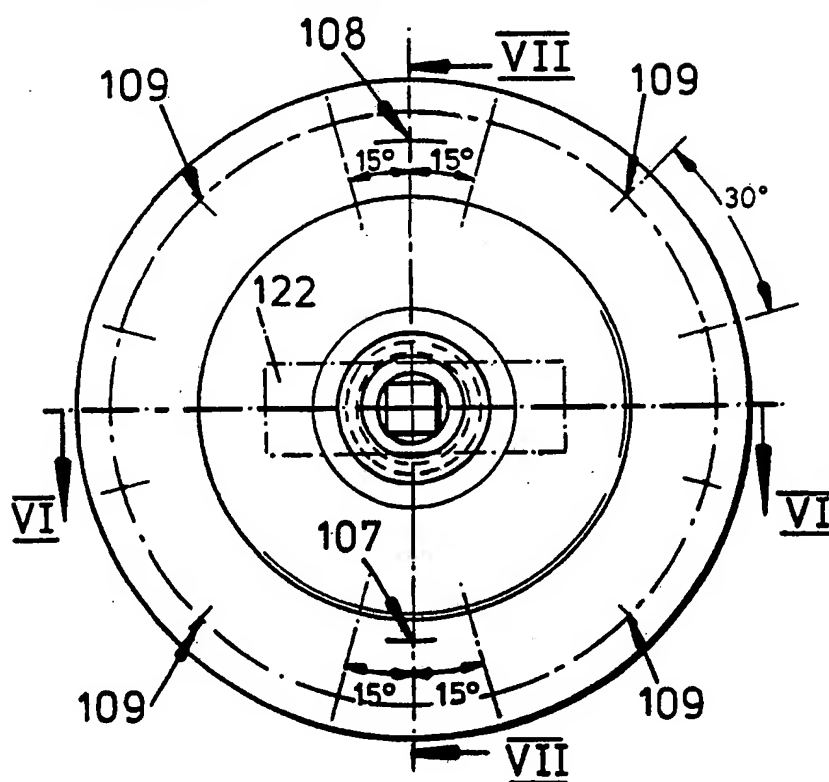


FIG. 5

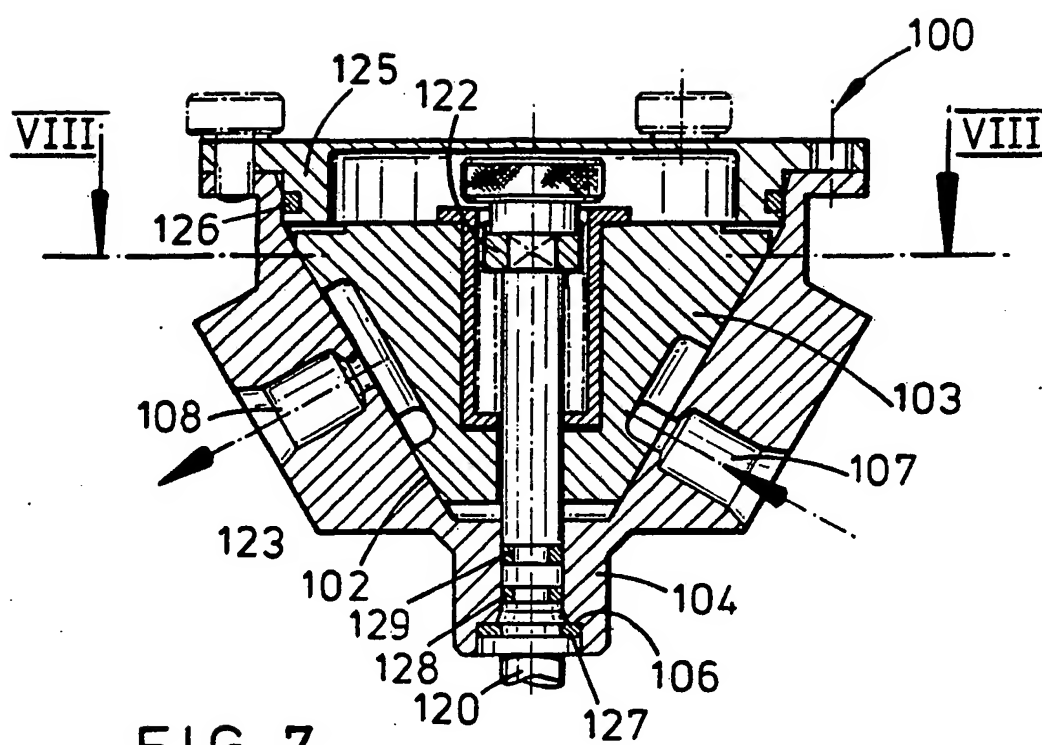


FIG. 7

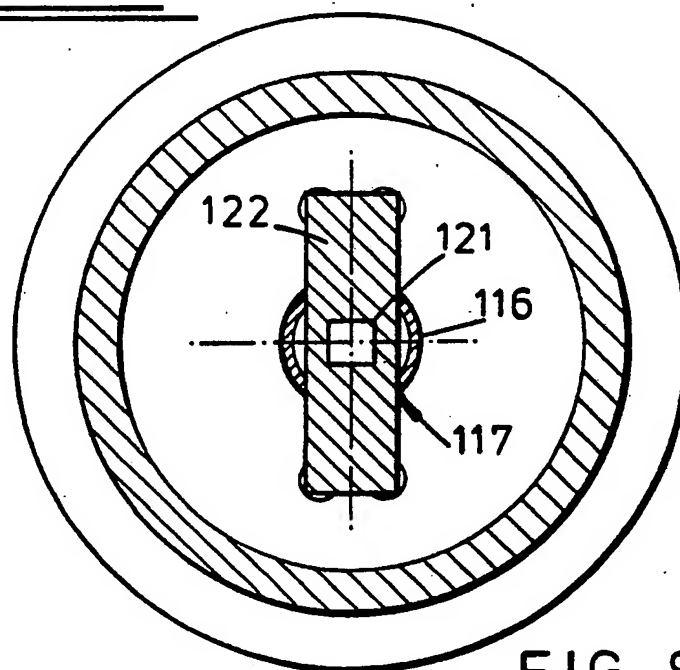
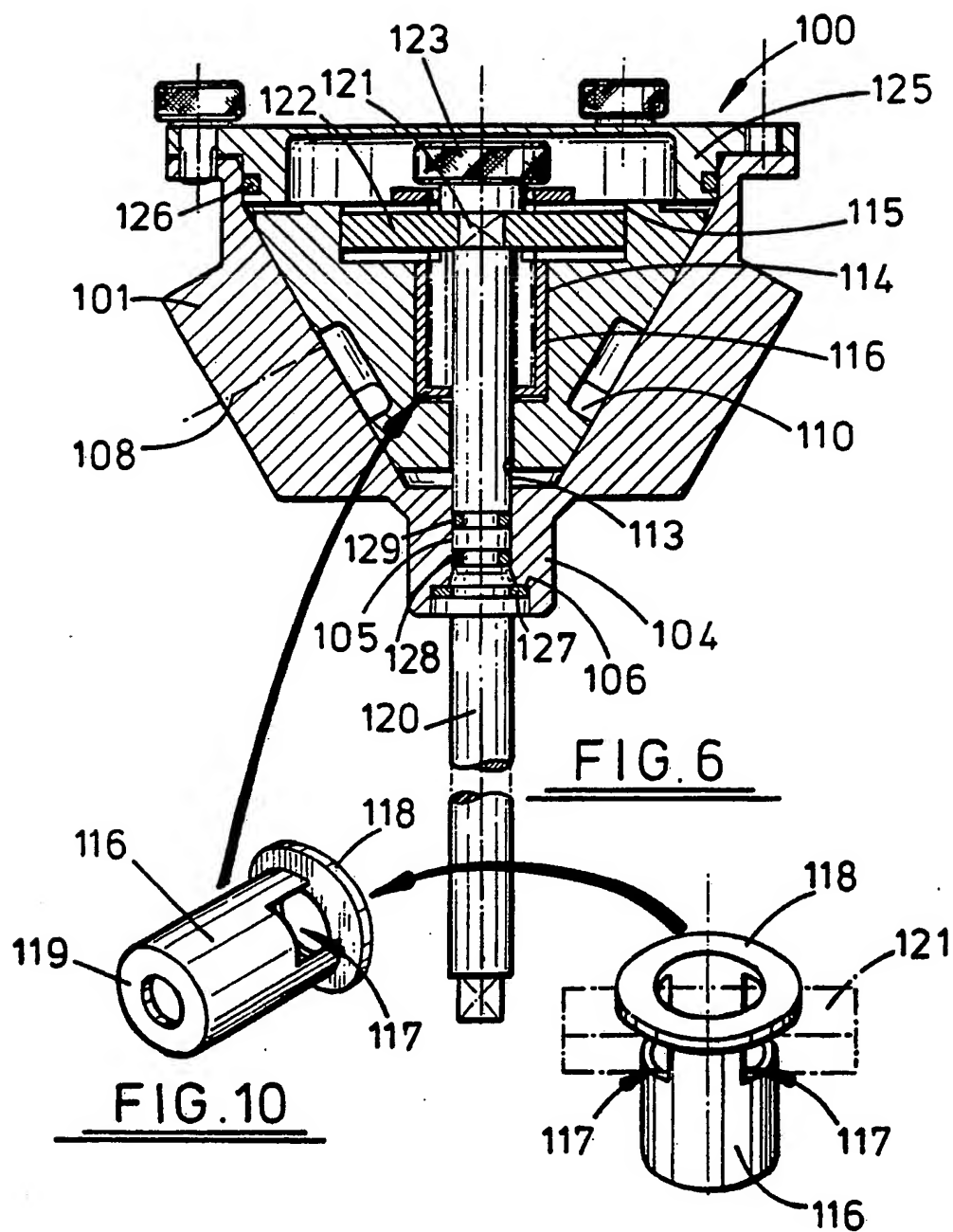


FIG. 8



REQUEST FOR RECTIFICATION PUBLISHED UNDER THE PROVISIONS
OF PCT RULE 91.1 (f)

As discussed with your Mr. Pennel and Mr. Pike, it has come to our attention that the Request form lodge with the above application did not include the customary sheet including Boxes IV and V, the latter of which includes the list of PCT countries.

We have been asked by Mr. Pike to present our submissions that, in spite of this omission, the application should be allowed to proceed with the filing date of 29 June and include all PCT countries as designations.

The Request as filed lists the names and addresses of seven individuals who are indicated as being "applicant and inventor" for "the United States of America only". Thus, the Request clearly designates the United States. The Request also includes three "corporate" entities which are in the category "applicant only" for "all designated states except the United States of America". In the absence of a specific list of countries, it is implicit in the Request form that the "corporate" entities are intended to be applicants in respect of all PCT countries (including regional designations) except the USA.

Article 11 of the Patent Co-operation Treaty states that the application will be accorded the International Filing Date as of its date of receipt (by the Receiving Office) provided that the International Applications contains inter alia the designation of at least one contracting state. As indicated above, the United States is expressly designated and the remaining PCT countries are implicitly designated. We have therefore complied with Article 11 (1).

The fact that all of the designated states were not specifically listed in the Request form at the time of filing the application is, we would submit, a correctable defect. Although Rule 4.9 of PCT states that the Contracting States shall be designated in the Request by their names, this does not in our view require that they be specifically so designated in the Request form as filed. To support this submission we would refer to Rules 4.1 (a) and 4.1.(d) which provide various requirements which the Request "shall contain" but it is clear from Article 14 that certain of these requirements need not be complied with in the Request form as filed and can be regarded as defects to be corrected later. In other words, the references to "shall" in Rules 4.1 and 4.9 cannot mean that the requirement must be complied with at the time of filing. In our submission it is sufficient that the Request form ultimately comply with the requirement within any time limit set by the office.

In summary therefore we would submit that the application explicitly designates the United States and implicitly designates all other PCT countries and that this is sufficient for the application to be accorded the filing date of 29 June. Further, the requirement under Rule 4.9 to list the Contracting States by name is a requirement which can be corrected post-filing and to this end we enclose the previously omitted sheet from the Request form.

We request an early decision in this matter. In the event that the decision is unfavourable, we request a Hearing.

The international application as filed on 29 June 1989 (29.06.89) claimed the priority of an earlier application filed in the United Kingdom on 29 June 1988 (29.06.88), application number 8815483. That priority claim was cancelled according to Rule 4.10(d) after 07 June 1989 (07.06.89) had been accorded as international filing date.

INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 89/00857

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁸ According to International Patent Classification (IPC) or to both National Classification and IPC IPC ⁵ : G 01 N 1/18																													
II. FIELDS SEARCHED <div style="text-align: center; border-top: 1px solid black; border-bottom: 1px solid black; margin: 5px 0;">Minimum Documentation Searched ⁷</div> <table style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 30%; border-bottom: 1px solid black;">Classification System</th> <th style="border-bottom: 1px solid black;">Classification Symbols</th> </tr> <tr> <td style="padding: 5px;">IPC⁵</td> <td style="padding: 5px;">G 01 N 1/00, F 16 K 11/00</td> </tr> </table> <div style="text-align: center; border-top: 1px solid black; border-bottom: 1px solid black; margin: 5px 0;">Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁶</div>			Classification System	Classification Symbols	IPC ⁵	G 01 N 1/00, F 16 K 11/00																							
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III. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹ <table style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 10%; border-bottom: 1px solid black;">Category ⁹</th> <th style="width: 70%; border-bottom: 1px solid black;">Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²</th> <th style="width: 20%; border-bottom: 1px solid black;">Relevant to Claim No. ¹³</th> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="padding: 5px;">GB, A, 1215086 (JONES) 9 December 1970 see page 5, right-hand column, line 90 - page 6, left-hand column, line 28; figure 6</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1,3,9,10</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">A</td> <td style="text-align: center; vertical-align: top; padding: 5px;">--</td> <td style="text-align: center; vertical-align: top; padding: 5px;">5,6,7</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">A</td> <td style="padding: 5px;">FR, A, 1549443 (POTASSE & ENGRAIS CHIMIQUE) 13 December 1968 see page 3, left-hand column, paragraph 3; figures</td> <td style="text-align: center; vertical-align: top; padding: 5px;">5,6</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">A</td> <td style="text-align: center; vertical-align: top; padding: 5px;">--</td> <td style="text-align: center; vertical-align: top; padding: 5px;">6,7</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">A</td> <td style="padding: 5px;">US, A, 1854307 (HAPGOOD) 19 April 1932 see page 2, left-hand column, lines 3-60; figures 2,3</td> <td style="text-align: center; vertical-align: top; padding: 5px;">7,8</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">A</td> <td style="padding: 5px;">GB, A, 1353747 (BRITTAN) 22 May 1974 see page 4, lines 28-35; claim 1</td> <td style="text-align: center; vertical-align: top; padding: 5px;">7,8</td> </tr> <tr> <td></td> <td style="text-align: center; padding: 5px;">--</td> <td></td> </tr> <tr> <td></td> <td style="text-align: center; padding: 5px;">./.</td> <td></td> </tr> </table>			Category ⁹	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³	X	GB, A, 1215086 (JONES) 9 December 1970 see page 5, right-hand column, line 90 - page 6, left-hand column, line 28; figure 6	1,3,9,10	A	--	5,6,7	A	FR, A, 1549443 (POTASSE & ENGRAIS CHIMIQUE) 13 December 1968 see page 3, left-hand column, paragraph 3; figures	5,6	A	--	6,7	A	US, A, 1854307 (HAPGOOD) 19 April 1932 see page 2, left-hand column, lines 3-60; figures 2,3	7,8	A	GB, A, 1353747 (BRITTAN) 22 May 1974 see page 4, lines 28-35; claim 1	7,8		--			./.	
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<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>¹⁰ Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p> </div> </div>																													
IV. CERTIFICATION <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; border-bottom: 1px solid black; padding: 5px;">Date of the Actual Completion of the International Search</td> <td style="width: 50%; border-bottom: 1px solid black; padding: 5px;">Date of Mailing of this International Search Report</td> </tr> <tr> <td style="padding: 5px;">27th October 1989</td> <td style="padding: 5px;">28. 11. 89</td> </tr> <tr> <td style="border-bottom: 1px solid black; padding: 5px;">International Searching Authority</td> <td style="border-bottom: 1px solid black; padding: 5px;">Signature of Authorized Officer</td> </tr> <tr> <td style="padding: 5px; text-align: center;">EUROPEAN PATENT OFFICE</td> <td style="padding: 5px; text-align: center;"> <div style="text-align: right; font-weight: bold; margin-top: 5px;">T.K. WILLIS</div> </td> </tr> </table>			Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	27th October 1989	28. 11. 89	International Searching Authority	Signature of Authorized Officer	EUROPEAN PATENT OFFICE	<div style="text-align: right; font-weight: bold; margin-top: 5px;">T.K. WILLIS</div>																			
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III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	US, A, 2309625 (ANTRELL) 2 February 1943 see page 2, claim 7; figures --	1,9
A	EP, A, 0244751 (GENERAL ELECTRIC CO.) 11 November 1987 see columns 11-12; claim 1; figure 3 -----	1

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.**

GB 8900857

SA 30370

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 17/11/89. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB-A- 1215086	09-12-70	None	
FR-A- 1549443	13-12-68	None	
US-A- 1854307		None	
GB-A- 1353747	22-05-74	None	
US-A- 2309625		None	
EP-A- 0244751	11-11-87	US-A- 4722830	02-02-88
		JP-A- 62278425	03-12-87